**Supplemental Table 33. Evidence Summary and Evidence to Decision Table for Rehabiliation/Mobilization Actionable Question**

**Question: Rehabilitation or mobilization (performed either in-bed or out-of-bed) compared to usual care in critically ill adults**

| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **rehabilitation or mobilization (performed either in-bed or out-of-bed)** | **usual care** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Hospital Mortality | | | | | | | | | | | | |
| 13 | randomised trials | not serious | not serious | not serious | serious a | none | 106/706 (15.0%) | 117/715 (16.4%) | **RR 0.93** (0.74 to 1.18) | **11 fewer per 1,000** (from 29 more to 43 fewer) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| MRC at ICU discharge | | | | | | | | | | | | |
| 6 | randomised trials | not serious b | serious c | not serious | serious d | none e | 147 | 157 | - | MD **6.24 higher** (1.67 higher to 10.82 higher) | ⨁⨁◯◯ LOW | CRITICAL |
| SF-36 (Physical Function) within 2 months | | | | | | | | | | | | |
| 4 | randomised trials | not serious | serious h | not serious | serious i | none | 156 | 147 | - | SMD **0.64 higher** (0.05 lower to 1.34 higher) | ⨁⨁◯◯ LOW | CRITICAL |
| PFIT at ICU discharge | | | | | | | | | | | | |
| 3 | randomised trials | not serious | not serious | not serious | serious j | none e | 109 | 100 | - | MD **0.19 lower** (0.69 lower to 0.31 higher) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| TUG at Hospital Discharge | | | | | | | | | | | | |
| 3 | randomised trials | not serious | not serious k | not serious | serious l | none e | 89 | 83 | - | MD **2.22 higher** (4.99 lower to 9.43 higher) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| Duration of Mechanical Ventilation | | | | | | | | | | | | |
| 11 | randomised trials | serious m | serious n | not serious | not serious | none e | 562 | 566 | - | MD **1.31 lower** (2.44 lower to 0.19 lower) | ⨁⨁◯◯ LOW | CRITICAL |
| Serious Adverse Event | | | | | | | | | | | | |
| 13 | observational studies | not serious | not serious | not serious o | not serious | dose response gradient | 20/12217 (0.16%) | not pooled | not pooled | see comment | ⨁⨁⨁◯ MODERATE | CRITICAL |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference; **SMD:** Standardised mean difference

a. We downgraded the quality of evidence for imprecision by one level, the CI contained both significant benefit and harm

b. Five RCTs were at low risk of bias, one RCT (Dantas 2012) risk of bias was unclear, a sensitivity analysis excluding this study did not affect the overall estimate, suggesting that the impact of risk of bias is minimal on this outcome

c. We downgraded the quality of evidence for inconsistency by one level, the I2= 57% and was not explained by our subgroup analyses

d. We downgraded the quality of evidence for imprecision, the CI included values below the minimally important difference threshold

e. We were not able to appropriately assess for publication bias due to small number of studies

f. We did not downgraded the quality of evidence for risk of bias, all studies were judged to be at high risk of bias

g. We downgraded the quality of evidence for inconsistency by two levels, the I2= 89% which is substantial, indicating that the point estimates differed greatly between studies

h. We downgraded the quality of evidence by one level for inconsistency, the I2 =85%

i. We downgraded the quality of evidence by one level for imprecision, the CI crosses the line of no effect

j. We downgraded the quality of evidence by one level for imprecision, the CI was wide including both significant benefit and harm

k. Although I2=36% we did not downgrade for inconsistency

l. We downgraded the quality of evidence for imprecision by one level, the CI contained both significant benefit and harm

m. We downgraded the quality of evidence by one level for risk of bias, two RCTs constituting > 50% of the weight in the analysis were at high risk of bias. In addition, there is the issue of competing risk between mortality and duration of ventilation which could have resulted in biased estimates

n. We downgraded the quality of evidence for inconsistency by one level, the I2=73% that is large and not explained by subgroup analysis

o. We downgraded the quality of evidence for indirectness by one level, the studies used different intensity and type of physiotherapy

p. 1. Morris et al. 2016 intervention arm

q. 1. We downgraded the quality of evidence by one level for indirectness, assumptions were made about number of sessions per patient which may have influenced the final estimates

r. No explanation was provided

|  |  |  |  |
| --- | --- | --- | --- |
| Question | | | |
| Should **rehabilitation or mobilization (performed either in-bed or out-of-bed)** vs. **usual care** be used for **critically ill adults**? | | | |
| **Population:** | critically ill adults | **Background:** |  |
| **Intervention:** | rehabilitation or mobilization (performed either in-bed or out-of-bed) |
| **Comparison:** | usual care |
| **Main outcomes:** | Hospital Mortality; MRC/MMC at ICU discharge; SF-36 with in 1 month of ICU admission; SF-36 (Physical Function) with in 2 months; PFIT at ICU discharge; TUG at 1 month; Duration of Mechanical Ventilation; Serious Adverse Event ( average 8 PT sessions per patient); Serious Adverse Event ( average 24 PT sessions per patient); |
| **Setting:** | Intensive Care Unit |

Assessment

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Judgement** | **Research evidence** | **Additional considerations** |
| Problem | **Is the problem a priority?**  ○ No ○ Probably no ○ Probably yes **● Yes** ○ Varies ○ Don't know | No research evidence was identified. |  |
| Desirable Effects | **How substantial are the desirable anticipated effects?**  ○ Trivial **● Small** ○ Moderate ○ Large ○ Varies ○ Don't know | No research evidence was identified. |  |
| Undesirable  Effects | **How substantial are the undesirable anticipated effects?**  ○ Large ○ Moderate ○ Small **● Trivial** ○ Varies ○ Don't know |  |
| Certainty of evidence | **What is the overall certainty of the evidence of effects?**  ○ Very low **● Low** ○ Moderate ○ High ○ No included studies | *See Appendix 1*  **The relative importance or values of the main outcomes of interest:**   | **Outcome** | **Relative importance** | **Certainty of the evidence (GRADE)** | | --- | --- | --- | | Hospital Mortality | CRITICAL | ⨁⨁⨁◯ MODERATE | | MRC/MMC at ICU discharge | CRITICAL | ⨁⨁◯◯ LOW | | SF-36 with in 1 month of ICU admission | CRITICAL | ⨁⨁◯◯ LOW | | SF-36 (Physical Function) with in 2 months | CRITICAL | ⨁⨁◯◯ LOW | | PFIT at ICU discharge | CRITICAL | ⨁⨁⨁◯ MODERATE | | TUG at 1 month | CRITICAL | ⨁⨁⨁◯ MODERATE | | Duration of Mechanical Ventilation | CRITICAL | ⨁⨁◯◯ LOW | | Serious Adverse Event ( average 8 PT sessions per patient) | CRITICAL | ⨁⨁⨁◯ MODERATE | | Serious Adverse Event (assuming average 24 mobility sessions per patient) | CRITICAL | ⨁⨁⨁◯ MODERATE | |  |
| Values | **Is there important uncertainty about or variability in how much people value the main outcomes?**  ○ Important uncertainty or variability ○ Possibly important uncertainty or variability **● Probably no important uncertainty or variability** ○ No important uncertainty or variability | No direct values and preferences studies available to address the specific question. However, a survey of families/visitors of critically ill patients showed that amongst the most important outcomes surviving ICU and shorter time on ventilator were ranked highly. [1] | Discussion with panelists, patients representative, and reviewing the indirect evidence all suggested that patients will probably value the benefits of receiving rehabilitation over potential serious adverse events |
| Balance of effects | **Does the balance between desirable and undesirable effects favor the intervention or the comparison?**  ○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison **● Probably favors the intervention** ○ Favors the intervention ○ Varies ○ Don't know | No research evidence was identified. |  |
| Resources required | **How large are the resource requirements (costs)?**  ○ Large costs **● Moderate costs** ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know | No research evidence was identified. | Implementation of rehabilitation/mobilization may require specific resources (i.e., specially trained personnel and/or equipment). Research studies and quality improvement reports indicate use of specific health care providers to deliver the rehabilitation/mobility interventions, including physical therapists, occupational therapists, nurses, or assistants. Training of these personnel may be required to meet the unique needs of critically ill patients. While some equipment, such as mobility aids (e.g., walkers or mechanical lifts), are available in most hospitals, other specialized equipment (e.g., in-bed cycle ergometers and neuromuscular electrical stimulation devices), is sometimes used and may represent additional costs. Hence, the resource requirements were determined to be “moderate costs.” |
| Certainty of evidence of required resources | **What is the certainty of the evidence of resource requirements (costs)?**  ○ Very low ○ Low **● Moderate** ○ High ○ No included studies | No research evidence was identified. |  |
| Cost effectiveness | **Does the cost-effectiveness of the intervention favor the intervention or the comparison?**  ○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison **● Probably favors the intervention** ○ Favors the intervention ○ Varies ○ No included studies | A financial model, based on actual experience and published data available prior to 2013 (predominantly from studies in medical ICUs), projects that investment in an ICU early rehabilitation program can generate net financial savings for U.S. hospitals. Even under the most conservative assumptions, the projected net cost of implementing such a program is modest relative to the substantial improvements in patient outcomes demonstrated by ICU early rehabilitation programs. [2]  In addition, a quasi-randomized trial in a single medical ICU in the U.S. noted that early ICU mobility does not increase costs (the average cost per patient was $44,302 for the Usual Care group and $41,142 for the Protocol group, p=0.262.) [3] |  |
| Acceptability | **Is the intervention acceptable to key stakeholders?**  ○ No ○ Probably no ○ Probably yes **● Yes** ○ Varies ○ Don't know | A survey of 33 RNs in a single institution suggest that common reasons to restrict mobility were patient-centered, including unstable vital signs, low respiratory or energy reserves, and risk to tubing or catheter integrity. Sedation, coma and agitation in patients are also barriers to mobility and progression. Mobility was an important intervention in planning daily work. [4]  A multidisciplinary study of 17 RNs, 12 PTs and 91 MDs at a single site (MICU) indicated that mechanical ventilation was not a barrier and that mobility was viewed as beneficial to patients.  Barriers reported by RNs were risk of self-injury, excessive work stress and nursing time or delays in usual work and prolonging work days are barriers to implementing mobility interventions by RNS  Barriers reported by PTs were limited time, staffing, and concern for staff-related injuries  Barriers reported by MDs were lack of staffing, excessive sedation, delirium and patient safety. [5]  Focus groups evaluating pre- and post-implementation of the ABCDE bundle in a single institution reported that the majority of participants viewed mobility as benefiting patient function and weaning. RNs perceived harm when mobility was imbedded in a bundle protocol and that there was not enough staff to do the labor-intensive mobility work. Nurses also identified inconsistency in practice among the ICU MDs/MDs not open to recommendations as a barrier. [6]  A qualitative study, which conducted interviews of 20 multi-disciplinary stakeholders regarding a rehabilitation program in a single medical ICU, indicated that 100% of participants believed that ICU-based rehabilitation improved patient outcomes and 95% reported increased job satisfaction related to the program. Regarding perceived barriers, 80% were concerned about increase workload, and 65% were mentioned safety concerns. [7]  A survey of patients and families suggest that physical therapy is perceived as acceptable and necessary to patients [8]  NO EVIDENCE FOR POLICY MAKERS provided by our group |  |
| Feasibility | **Is the intervention feasible to implement?**  ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know | No research evidence was identified. |  |

## Summary of judgements

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | **Small** | Moderate | Large |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | **Trivial** |  | Varies | Don't know |
| **Certainty of evidence** | Very low | **Low** | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | **Probably favors the intervention** | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | **Moderate costs** | Negligible costs and savings | Moderate savings | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | **Moderate** | High |  |  | No included studies |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | **Probably favors the intervention** | Favors the intervention | Varies | No included studies |
| **Equity** | Reduced | Probably reduced | Probably no impact | Probably increased | Increased | Varies | Don't know |
| **Acceptability** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Feasibility** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |

**Should rehabilitation or mobilization (performed either in-bed or out-of-bed) vs. usual care be used in critically ill adults?**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Type of recommendation** | |  |  |  |  |  | | --- | --- | --- | --- | --- | | Strong recommendation against the intervention | Conditional recommendation against the intervention | Conditional recommendation for either the intervention or the comparison | Conditional recommendation for the intervention | Strong recommendation for the intervention | | ○ | ○ | ○ | ● | ○ | |
| **Recommendation** | We suggest rehabilitation or mobilization (performed either in-bed or out-of-bed in the ICU) in adult critically ill patients. |
| **Subgroup considerations** | Early vs. Late - data not enough to perform subgroup analysis |
| **Monitoring and evaluation** | Safety criteria |
| **Research priorities** | Evaluation of measurement properties of outcomes measures for testing the short- and long-term effects of ICU-based rehabilitation and mobility is still evolving and many existing studies have not used instruments that have been evaluated in the ICU patient population.  Subgroup of patients that may benefit vs. not are still not well defined including understanding the roles/effects of pre-ICU functional status vs. ICU-based immobility vs. muscle wasting and nerve/muscle dysfunction related to critical illness that may be less modifiable from mobilization/rehabilitation interventions.  Understanding the differences in outcomes according to the type of intervention, the timing of starting the intervention, along with frequency, duration and intensity of each session and expertise/training of personnel delivering intervention, with greater measurement and reporting of these issues for both intervention and control groups.  Methods to measure stress and distress in nonverbal patients are needed to better understand the patient experience of receiving mobility and rehabilitation while mechanically ventilated in the ICU. |
| **voting comments** | I agree with the outcome measure being 'the patient' but don't understand why Family/ health systems are outcomes, too broad.  Recommendation suggests that rehab or mobilization beneficial for family and health systems? not confirmed in the included studies Cannot understand: ’or similar interventions with reduced duration, frequency or a later onset’. Can minimal duration, frequency and onset be defined? |

References

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